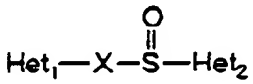
PCT/SE97/01093
11 -09- 1998

Amended claims

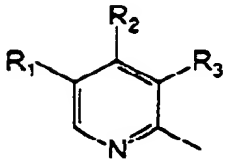
1. An administration regimen for improved inhibition of gastric acid secretion characterized in that an extended blood plasma profile of a H^+, K^+-ATPase inhibitor is obtained and that said H^+, K^+-ATPase inhibitor is a compound with the formula I



I

wherein

Het_1 is



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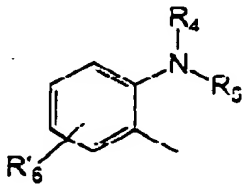
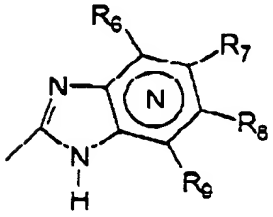


Het_2 is



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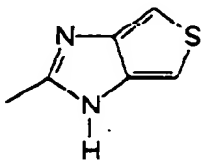
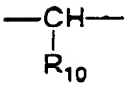


X –



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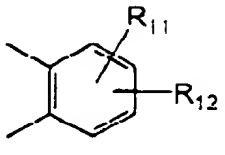


and wherein

AMENDED SHEET

N in the benzimidazole moiety means that one of the ring carbon atoms substituted by R_6-R_9 optionally may be exchanged for a nitrogen atom without any substituents;

R_1, R_2 and R_3 are the same or different and selected from hydrogen, alkyl, alkoxy optionally substituted by fluorine, alkylthio, alkoxyalkoxy, dialkylamino, piperidino, morpholino, halogen, phenyl and phenylalkoxy;

R_4 and R_5 are the same or different and selected from hydrogen, alkyl and aralkyl;

R_6' is hydrogen, halogen, trifluoromethyl, alkyl and alkoxy;
R_6-R_9 are the same or different and selected from hydrogen, alkyl, alkoxy, halogen, halo-alkoxy, alkylcarbonyl, alkoxycarbonyl, oxazolyl, trifluoroalkyl, or adjacent groups R_6-R_9 form ring structures which may be further substituted;

R_{10} is hydrogen or forms an alkylene chain together with R_3 and

R_{11} and R_{12} are the same or different and selected from hydrogen, halogen or alkyl.

2. An administration regimen according to claim 1 characterized in that the H^+, K^+-ATPase inhibitor is a compound selected from the group of omeprazole, an alkaline salt of omeprazole, the (-)-enantiomer of omeprazole and an alkaline salt of the (-)-enantiomer of omeprazole.

3. An administration regimen giving an extended blood plasma profile of a H^+, K^+-ATPase inhibitor according to any of claims 1 and 2 characterized in that the extended plasma profile is obtained by two or more consecutive oral administrations of a unit dose of the H^+, K^+-ATPase inhibitor with 0.5 - 4 hours intervals.

4. An administration regimen giving an extended blood plasma profile of a H^+, K^+-ATPase inhibitor according to claim 1 characterized in that the extended plasma profile is obtained by oral administration of a unit dose of a pharmaceutical

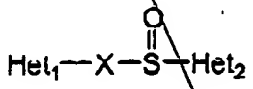
PCT/SE97/01900
11 -08- 1998

preparation which releases the drug for absorption in two or more discrete pulses separated in time by 0.5 - 4 hours.

5. An administration regimen according to claim 1, characterized in that the extended plasma profile is obtained by oral administration of a unit dose of a pharmaceutical preparation which releases the H^+, K^+-ATPase inhibitor for absorption with an almost constant rate during an extended time period.

6. An administration regimen according to any of claims 1 - 5 characterized in that the extended plasma profile is received during 2 - 12 hours.

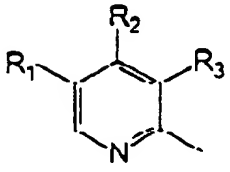
7. An oral pharmaceutical composition giving an extended blood plasma profile of a H^+, K^+-ATPase inhibitor, characterized in that the H^+, K^+-ATPase inhibitor is a compound with the formula I



I

wherein

Het_1 is



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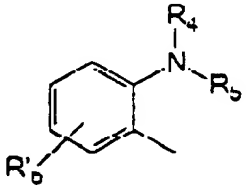

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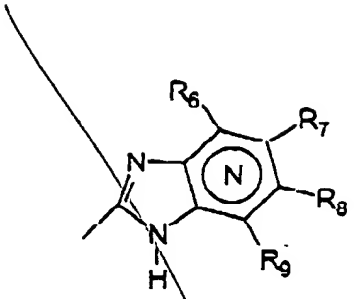

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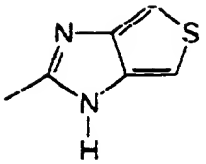

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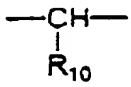

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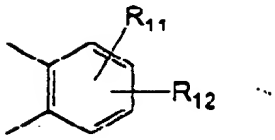

wherein

N in the benzimidazole moiety means that one of the ring carbon atoms substituted by R_6-R_9 optionally may be exchanged for a nitrogen atom without any substituents;

R_1, R_2 and R_3 are the same or different and selected from hydrogen, alkyl, alkoxy optionally substituted by fluorine, alkylthio, alkoxyalkoxy, dialkylamino, piperidino, morpholino, halogen, phenyl and phenylalkoxy;

R_4 and R_5 are the same or different and selected from hydrogen, alkyl and aralkyl;

R_6' is hydrogen, halogen, trifluoromethyl, alkyl and alkoxy;
R_6-R_9 are the same or different and selected from hydrogen, alkyl, alkoxy, halogen, halo-alkoxy, alkylcarbonyl, alkoxycarbonyl, oxazolyl, trifluoroalkyl, or adjacent groups R_6-R_9 form ring structures which may be further substituted;

R_{10} is hydrogen or forms an alkylene chain together with R_3, and

R_{11} and R_{12} are the same or different and selected from hydrogen, halogen or alkyl.

8. An oral pharmaceutical preparation according to claim 7, characterized in that the H^+, K^+-ATPase inhibitor is a compound selected from the group of omeprazole, an

alkaline salt of omeprazole, the (-)-enantiomer of omeprazole and an alkaline salt of the (-)-enantiomer of omeprazole.

9. An oral pharmaceutical preparation giving an extended blood plasma profile of a H^+, K^+-ATPase inhibitor according to claim 7 characterized in that the pharmaceutical preparation releases the drug for absorption in two or more discrete pulses separated in time by 0.5 - 4 hours.

10. An oral pharmaceutical preparation according to claim 7, characterized in that the pharmaceutical preparation releases the H^+, K^+-ATPase inhibitor for absorption with an almost constant rate during an extended time period.

11. An oral pharmaceutical preparation giving an extended blood plasma profile of a H^+, K^+-ATPase inhibitor according to any of claims 7 - 10 characterized in that the ~~extended plasma~~ profile is received during 2 - 12 hours.

12. Use of an oral pharmaceutical composition as claimed in any of claims 7 - 10 in the manufacture of a medicament with improved inhibition of gastric acid secretion.

13. Use of an oral pharmaceutical composition as claimed in any of claims 7 - 10 in the manufacture of a medicament with improved therapeutic effect in the treatment of gastrointestinal disorders associated with excess acid secretion.

14. Use of H^+, K^+ - ATPase inhibitor with the formula I defined in claim 1, for the preparation of a pharmaceutical composition with extended release.

15. A method for improving inhibition of gastric acid secretion which comprises administering to a patient in need thereof, an oral pharmaceutical composition as claimed in any of claims 7 - 10.

16. A method for improving the therapeutic effect in the treatment of gastrointestinal disorders associated with excess acid secretion which comprises

administering to a patient in need thereof, an oral pharmaceutical composition as claimed in any claims 7 - 10.

17. A method for receiving an extended plasma profile of a H^+, K^+- ATPase inhibitor by administering to a patient in need thereof a pharmaceutical preparation with extended release of a H^+, K^+- ATPase inhibitor as defined in claim 1.

add 5

add B

add C

add D